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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,161	03/04/2002	Yuichi Oku	MIT-C205	9188

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,161	OKU ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,9-23 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _ is/are allowed.

6)☒ Claim(s) *1,4-7,9-23 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed July 29, 2005 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 9-11, 13, 14, 16, 18, 20-23 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al (US 2003/0118595).

Niemeyer et al disclose methods and bioconjugates for determining a target analyte of interest. Niemeyer et al disclose a solid phase (chip) having oligonucleotides (R3) immobilized on the solid phase (p. 14, paragraph 0127, lines 1-5). Niemeyer et al disclose a bioconjugate (receptor II) comprising DNA-STV hybrids (DNA (B3)- STV (strepavidin, R2) bound to a biotinylated (B2) antibody (L2) (p. 14, para. 0127, lines 9-10). Niemeyer et al disclose that the solid phase oligonucleotides (R3) is capable of binding to the DNA (B3) of the DNA-STV hybrid. Niemeyer et al disclose that the bioconjugate binds to a target analyte such as an antibody (p. 14, para. 0127, lines 11-13). Niemeyer et al disclose that the target can be detected by another conjugate (receptor I). Niemeyer et al disclose that this conjugated compound comprises biotinylated (B1) antibody (L1) combined with streptavidin (R1) coupled to nucleic acid (M) (p. 8, para. 0079, lines 43-60). Niemeyer et al disclose that the bioconjugates can be packaged into a kit (p. 2, para. 0017). Niemeyer et al disclose that the solid phase can be comprised of cellulose (p. 4, para. 0044) or a nitrocellulose membrane (p. 8, para. 0075). Niemeyer et al also disclose that the target analyte can be a nucleic acid (p. 8) and that conjugated nucleic acids can be used as detection reagents.

With respect to claim 13 since Niemeyer et al disclose the same substances B1, R1, B2 and R2 as applicant. It is inherent that the dissociation constant be from 10^{-8} to 10^{-16} (M).

Niemeyer et al differ from the instant invention in failing to specifically teach the solid phase conjugate is stored within the kit separate from at least receptor II.

Niemeyer et al discloses the claimed invention except for the solid phase conjugate separate from the receptor II. It would have been obvious to one having ordinary skill in the art at the time the invention was made to form the solid phase conjugate and receptor II as separate components and place them into the kit separately, since it has been held that constructing a formerly integral structure in various elements involves only routine skill in the art. *Nerwin v. Erlichman,* 168 USPQ 177, 179.

With respect to claim 28 Niemeyer et al discloses that the receptor I and receptor II are different reagents and used in a sequential manner and thus one of ordinary skill in the art would recognize that the reagents are separate within the kit of Niemeyer et al.

5. Claims 4-7 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al (US 2003/0118595) in view of Bayer et al (Immunoassay, edited by Diamandis et al, Chapter 11, The Avidin-Biotin System, 1996, pgs 237-267).

See above for the teachings of Niemeyer et al.

Niemeyer et al differ from the instant inventions in failing to specifically teach the R1 or R2 has a plurality of binding points with respect to B1 or B2, and a plurality of ligands L1 or L2 are bound to the R1 substances the substance B1.

Bayer et al disclose that avidin (R1 or R2 of Niemeyer) (interchangeable with strepavidin, p. 238) occurs in solution as a tetramer and thus has four binding biotin-binding sites per molecule (p.238). Niemeyer et al disclose that a plurality of

biotinylated probes such as biotinylated (B1 or B2) antibodies (L1 or L2) can bound to avidin (R1 or R2) (pgs 251-252). Bayer et al disclose that this provides for the introduction of preformed complexes and that the signals achieved using complexes are often superior to those achieved using conjugates (p. 251-252).

It would have been obvious to incorporate a plurality of biotinylated antibodies such as taught by Bayer et al into the method and kit of Niemeyer et al because Niemeyer et al specifically teaches the use of avidin – biotin systems and Bayer et al teach these systems provide for the introduction of preformed complexes and that the signals achieved using complexes are often superior to those achieved using conjugates

With respect to claims 5 and 7 as instantly recited since the combination of Niemeyer et al and Bayer et al disclose the same bioconjugates as recited in the claims the bioconjuates of Niemeyer et al and Bayer et al would appear to have plural types of reactivity. Further, Niemeyer et al disclose that the ligand can be a polyclonal antibody (p. 7) which binds to different epitopes on an antigen. Therefore, it appears that

With respect to claim 19 since Bayer et al teaches that avidin and streptavidin are interchangeable and are actually different molecules. It would have been obvious to one of ordinary skill in the art to replace one with the other in one of the receptor molecules because it is known in the art that avidin is an alternative for strepavidin and vice versa.

6. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al in view of Ghosh et al (US 5,237,016).

See above for the teachings of Niemeyer et al.

Niemeyer et al differ from the instant invention in failing to specifically teach the analyte A is DNA and the ligands L1 and L2 are complementary to different portions of the analyte A.

Ghosh et al disclose the detection of nucleic acid such as DNA. Ghosh et al disclose the use of oligonucleotide probes (ligands) to detect the nucleic acid. Ghosh et al disclose that the first oligonucleotide is complementary to at least a region of the nucleic acid and that the second oligonucleotide is complementary to a different region of the nucleic acid (col 1- col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate oligonucleotides into the method of Niemeyer et al because Niemeyer et al specifically teaches that nucleic acids can be the target and is generic with respect to the reagents to be used in this assay. Further, Niemeyer et al is generic with respect to the nucleic acid that is to be detected and one would use the appropriate reagent, i.e. oligonucleotides to detect the desired analyte, in this case DNA.

7. Claims 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al in view of Billing-Medel et al (US 2002/0142371).

See above for the teachings of Niemeyer et al.

Niemeyer et al differ from the instant invention in failing to specifically teach that the B1 and/or the substance B2 and wherein the substance R1 and/or the substance R2

is selected from the group consisting of DNA, RNA, antigen, antibody, lectin, glycoprotein, and sugars.

Billing-Medel teach assays in which specific binding members are used. Billing Medel teaches that specific binding member is a member of a specific binding pair. That is two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Billing-Medel teaches that antigen and antibody specific binding pairs are common in immunoassays and that other specific binding pairs include biotin and avidin, and carbohydrates and lectins.

It would have been obvious to one of ordinary skill in the art to incorporate antigen/antibody pairs as taught by Billing-Medel et al into the method of Niemeyer et al because Billing-Medel et al teaches that the use of antigen/antibody pairs are known in the art. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antigen/antibody pairs as taught by Billing-Medel et al into the method and kit of Niemeyer et al.

8. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al in view of Millipore (A Short Guide to Developing Immunochromatographic Test strips, pp. 1-36, Nov. 1996).

See above for Niemeyer et al.

Niemeyer et al differs from the instant invention in failing to teach the marker is detected as a line.

Millipore disclose nitrocellulose membranes (same as taught by Niemyer et al) as solid supports used in assays. Millipore teaches that the reagents used to capture a

target are immobilized into the formation of a line on the membrane and that formation of a line caused by detection reagents capture within this region indicates the presence of the target.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a solid phase system as taught by Millipore with the method and reagents of Niemeyer et al because Niemeyer et al specifically teaches that their methods can use nitrocellulose supports and visual detection reagents and Millipore shows that the formation of a colored line is well known in the art of assays. Therefore one of ordinary skill in the art would have a reasonable expectation of success incorporating a solid phase system comprising capture reagents immobilized in the formation of a line with the method and reagents of Niemeyer et al.

Response to Arguments

9. Applicant's arguments filed July 29, 2005 have been fully considered but they are not persuasive.

Applicant argues that claim 1 has been amended to include the limitation of claim 8 and thus the rejection for anticipation, not applied to claim 8 is considered moot. Examiner agrees that the anticipation rejection has been overcome by this amendment. However, claim 8 was previously rejected as obvious over Niemeyer et al and the obvious rejection of claim 8 has now been incorporated with claim 1 (see above for the 103 rejection concerning claim 1).

With respect to claims 4, 8, and 19, Applicant argues that even if avidin is used as R1 or R2 of Niemeyer, with the plurality of biotinylated probes bound thereto, the teachings of Niemeyer so modified are not suggestive of a kit wherein a solid phase conjugate is stored separate from another reactant. This is not found persuasive because of the 103 rejection above concerning claim 1.

Applicant's arguments with respect to claim 12 have been considered but are moot in view of the new ground(s) of rejection. Applicant's amendment to claim 12 necessitated the new grounds of rejection.

Applicant argues that claims 15 and 17 for obviousness over Niemeyer et al in view of Billing-Medal et al, is traversed for the reason that these claims depend from claim 1 and Niemeyer et al, modified in the allegedly obvious manner in view of Billing-Medal et al, would still fail to meet the limitations of claim 1. This is not found persuasive because of the 103 rejection above of claim 1. Thus it is the Examiner's position that the combination of Billin-Medal et al and Niemeyer et al reads on the instantly recited claims.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
September 30, 2005

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09/30/05